

isolated human skeletal myoblasts; and
isolated human fibroblasts,
the composition being substantially free of myotubes.

46. The composition of claim 43 or claim 44, wherein the composition is cultured *in vitro* for at least 7 days.

47. The composition of claim 43 or claim 44, which composition comprises cells that have been cultured *in vitro* for fewer than 20 population doublings.

48. The composition of claim 43 or claim 44, which composition comprises a collection of isolated cells consisting essentially of skeletal myoblasts and fibroblasts.

49. The composition of claim 48, which composition comprises a collection of isolated cells consisting essentially of human skeletal myoblasts and human fibroblasts.

Remarks

As discussed in the interview, Applicant respectfully submits that Allen does not teach or suggest compositions that are substantially free of myotubes. For instance, on page 528, Allen describes their standard 4 day cultures as containing "many myotubes". Also, throughout the reference, even the quantitation of satellite cells in their cultures is reported as the percentage of "mononucleated cells", clearly indicating that multinucleated myotubes were present in their earlier cultures, and were excluded from their percentage calculations.

Applicant has therefore specified, as agreed in the interview, that the claimed compositions are substantially free of myotubes. Support for this language can be found, for example, in the definition of "skeletal myoblasts" in the present specification, which definition describes the cells as "a precursor of myotubes and skeletal muscle fibers", and specifies that "such cells have one nucleus". The inventive compositions, therefore, are those that contain cells that *have the ability to become* myotubes, but have not yet formed myotubes. Consistent with this, the application points out that longer-term cultures can result in compositions that are

less desirable for transplantation purposes (see, for example, Examples 4 and 5), at least partly because some myoblasts in the cultures may have fused to form myotubes; myotubes do not survive as well as myoblasts in the transplant.

In addition, Applicant has provided dependent claims specifying compositions that contain at least 5% fibroblasts. Applicant respectfully submits that Allen does not teach or suggest compositions that lack myotubes and contain at least 5% fibroblasts.

Applicant has also submitted dependent claims specifying that the recited compositions are grown *in vitro* for at least 7 days. The Examiner considered Allen to report 10-20 day cultures, but Applicant respectfully points out that the 21 day growth period mentioned in Allen (pg. 526) was for *colonies*, not for collections of cells including satellite cells and fibroblasts. Other studies reported by Allen included 24 hr, 48 hr, or 4 day growth period, and those cultures, as noted above, included myotubes.

Applicant has further submitted dependent claims reciting human cells. Applicant respectfully submits that the procedure described by Allen for preparing cell compositions clearly gives different results (i.e., different percentages of satellite cells, fibroblasts, myotubes, etc) for cells of different origins. The Allen paper itself reports very different results for rat cells as compared with bovine cells. In fact, the paper describes their own techniques as being useful in the study of *rat* satellite cell cultures only (see Abstract, for example). Thus, even if Allen could provide teachings of cultures comprising *rat* skeletal myoblasts and fibroblasts, those teachings could not be extended to human cells. By contrast, the procedures described in the present application are equally applicable to human cells and have been demonstrated to produce the claimed compositions of human cells when so applied.

Applicant thanks both Examiners for their thoughtful work on this case, and looks forward to receiving a Notice of Allowance.

It is Applicant's understanding that there are no fees associated with this matter. Should this understanding be in error, please charge any fees to our Deposit Account No. 03-1721.

Respectfully submitted,

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Brenda Herschbach Jarrell, Ph.D.
Registration No. 39,223

Attorney for Applicant
CHOATE, HALL & STEWART
53 State Street
Boston, MA 02109
Telephone: 617-248-5000
Facsimile: 617-248-4000

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Brenda Herschbach Jarrell

Appendix A
Version With Markings to Show Changes Made

Please cancel all pending claims, and replace with:

43. A composition comprising:
isolated skeletal myoblasts; and
isolated fibroblast cells,
the composition being substantially free of myotubes.
44. The composition of claim 43, which composition comprises at least 5% fibroblasts.
45. The composition of claim 43 or claim 44, comprising:
isolated human skeletal myoblasts; and
isolated human fibroblasts,
the composition being substantially free of myotubes.
46. The composition of claim 43 or claim 44, wherein the composition is cultured *in vitro* for at least 7 days.
47. The composition of claim 43 or claim 44, which composition comprises cells that have been cultured *in vitro* for fewer than 20 population doublings.
48. The composition of claim 43 or claim 44, which composition comprises a collection of isolated cells consisting essentially of skeletal myoblasts and fibroblasts.
49. The composition of claim 48, which composition comprises a collection of isolated cells consisting essentially of human skeletal myoblasts and human fibroblasts.



Appendix B
Pending Claims After Entrance of Present Amendment

43. A composition comprising:
isolated skeletal myoblasts; and
isolated fibroblast cells,
the composition being substantially free of myotubes.
44. The composition of claim 43, which composition comprises at least 5% fibroblasts.
45. The composition of claim 43 or claim 44, comprising:
isolated human skeletal myoblasts; and
isolated human fibroblasts,
the composition being substantially free of myotubes.
46. The composition of claim 43 or claim 44, wherein the composition is cultured *in vitro* for at least 7 days.
47. The composition of claim 43 or claim 44, which composition comprises cells that have been cultured *in vitro* for fewer than 20 population doublings.
48. The composition of claim 43 or claim 44, which composition comprises a collection of isolated cells consisting essentially of skeletal myoblasts and fibroblasts.
49. The composition of claim 48, which composition comprises a collection of isolated cells consisting essentially of human skeletal myoblasts and human fibroblasts.

